IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Atty. Docket: KUMAZAWA1

In re Application of:	)	Conf. No.: 2023
	)	
Yoshio KUMAZAWA et al.	)	Examiner S. Y. Goon
	)	
Appln. No.: 10/553,695	)	Art Unit: 1623
	)	
Filed: August 7, 2006	)	Washington, D.C.
	)	
For: A CELL ACTIVATOR	)	

DECLARATION UNDER 37 CFR §1.132

Honorable Commissioner for Patents
U.S. Patent and Trademark Office
Customer Service Window
Randolph Building, **Mail Stop Amendment**
401 Dulany Street
Alexandria, VA 22314

Sir:

I, Masahiro Kubota, hereby declare and state as follows:

1. I have a Master degree from Kitasato University, Factory of Basic Life Science, Course of Bioscience in March, 2002.

2. I have been engaged in research and development of pharmaceutical products and food products at Foodchemifa Co., Ltd., which is an assignee of the instant application.

3. I am not one of the inventors listed on the instant application.

4. I have reviewed the file history of Application No. 10/553,695, including the specification, claims, and the non-final Office Action of November 9, 2009. In doing so, I have reviewed the anticipation rejections of claims 30, 32, and 34 as being anticipated by Kawahara et al. (PG Pub No. US 2002/0037291 A1) and separately by

Murata et al. (US 6,348,201). I have also reviewed the obviousness rejections of claims 30, 32, and 34 as being unpatentable over Kawahara (US 5,672,693) (hereinafter referred to as the '693 patent) as evidenced by Laloux et al. (The Journal of Immunology, vol. 168, pp. 3251-3258, 2002), in view of Nicoara et al. (Timisoara Medical Journal, vol. 53, nos. 3-4, pp. 303-307, 2003). Based on my review, it is my opinion that the claimed method of the instant application is novel and patentable for the following reasons.

5. In support of the rejections, the Examiner argues that the prior art teachings of methods of administering glycolsphingolipids (hereinafter "GSL") "are the same or nearly the same" as the claimed methods, and thus, the prior art methods and the GSL disclosed therein would necessarily have the same mechanism of action and produce the same effects, as the claimed method. I disagree.

First, the methods in the prior art are not the same as the claimed methods. The cited references only contemplate external uses involving topical application of GSL to the skin for completely different purposes than the claimed method. By contrast, the methods of claims 30, 32, and 34 require that the administering step results in: (i) activating NKT cells, (ii) accelerating IL-4 production, and (iii) accelerating IFN-γ production. In other words, the claimed methods require administering GSL in a manner, for example, by intravenous injection, infusion, oral ingestion, or intraperitoneal injection, to achieve this effect. Moreover, it is my opinion, as

explained herein, that the prior art methods involving external/topical application are not capable of achieving this effect due to differences in route of administration and differences in the mechanism of action for different GSLs.

Second, there is no hint or suggestion in the references that GSL activates NKT cells, and accelerates IL-4 production and IFN-γ production, regardless as to whether the GSL is administered externally (for topical use) as in the references or by internal use, such as injection. The references are silent in this matter.

Third, the arguments in the Office Action in support of the rejections rely on the assumptions that GSL's have the same mechanism of action, and that the prior art method of external topical application to the skin would necessarily produce the same mechanism of action with the same results of the claims. However, it is my opinion that these assumptions are incorrect.

There is no reasonable basis to assume that all GSL's have the same mechanism of action. Nor is there a reasonable basis to believe that topical application of GSL produces the same effects.

As to mechanism of action, it is known that different kinds of GSL effectively work by different mechanisms of action, as evident by the disclosure in Krziwon et al. (Infection and Immunity, vol. 63, no. 8, pp. 2899-2905 (August 1995)), a copy of which is submitted with the response. In Krziwon's mechanism, GSL stimulates monocular cells or monocytes (Table 1 of Krziwon). It can be recognized from Fig. 2 of Krziwon that the mechanism disclosed in Krzion is distinctly

different from that of the claimed invention. This is because the mechanism in Krziwon is effective for GSL-1, which corresponds to GSL-1 of the invention, but the mechanism in Krziwon is not effective for GSL-4A, which also corresponds to GSL-2 of the present invention. In contrast, both GSL-1 and GSL-2 work as a ligand of CD1, thereby activating NKT cell (as shown in Example 1 of the present application). Based on this, it is my opinion that the GSL in the method of the prior art references necessarily does not have the same mechanism of action with the same results, as required in the claims.

Furthermore, the differences in the objectives and the routes of administering GSL between the claimed method and the prior art methods also support the above conclusion. Kawahara et al. and Murata et al. both disclose only an external composition for external/topical application to the skin or the head. Though the references do briefly mention the word "pharmaceutical" in an alternative embodiment, the remainder of the references, and in particular, Kawahara et al. and Murata et al. only discuss and exemplify external cosmetic uses that are topically applied to the skin.

Thus, it should be clear that the Kawahara et al. and Murata et al. references only contemplate and disclose cosmetic uses involving topical applications only for applying GLS on the skin or head for completely different purposes and effects.

As to topical application, it should be understood that topical application of a substance generally results in a local effect,

as the substance is applied directly where its action is desired. Moreover, it is my opinion that topical administration to skin, as disclosed in the cited references, cannot achieve the results of claims. In this regard, it is well-known that skin is damaged when an intercellular substance such as ceramide decreases. Kawahara et al. and Murata et al. use GSL as a supplement of this intercellular substance. GSL include ceramide, and therefore, GSL would work as alternative to the intercellular substance in skin and thus recover the damaged skin. However, NKT activation is caused by directly acting on CD1, which is completely different as compared to use of GSL as a supplement of an intercellular substance, i.e., ceramide, to repair damaged skin.

Further, it should be noted that in the second Kawahara et al. reference, i.e., Kawahara et al. (US 5,672,693) cited in the obviousness rejection, GSL does not directly work with CD1d. This is because the '693 patent discloses that "the glycoliopid of the present invention possesses a B cell mitogen activity" (See Column 7, lines 45-54 of Kawahara, the '693 patent). That is, the '693 patent discloses that a certain kind of GSL works as mitogen of B cell. It is well-known that mitogen encourages a cell such as a B cell or a T cell to commence cell division, thereby triggering mitosis. It is also well-known that mitogen acts on B cells or T cells, as evidenced by the submitted copy of the Wikipedia definition of mitogen. Based on this, it is apparent that, in the '693 patent, GSL acts on B cell, and therefore, GSL cannot directly work with CD1d.

All of this is further evidence that the method and GSL in the teachings of the cited references have different mechanisms of action, as compared to the claimed invention. Thus, it is my opinion that that GSL's do not all have the same mechanism of action, and in fact, in the present case, they have different mechanisms of action. It is also my opinion that the references only contemplate topical application of GSL, and this topical application cannot produce the same effects, as recited in the claims. In other words, the cited references do not contemplate administering GSL internally, wherein it is used as a ligand of DC1 to activate NKT cells, to result in the production of large amounts of IL-4 and IFN-γ, as recited in the claims.

6. I further declare that all statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of this application or any patent issuing thereon.

Date: February 15, 2010

Masahiro KUBOTA

Masahiro KUBOTA